December 15, 1957

Dear Professor Fredericq:

The CIBA symposium volume arrived here recently, and I had an opportunity again to study your most interesting paper on the genetics of colicinogeny. I am really indebted to you for having prepared this lucid summary, for I must confess I had not grasped the full significance of your studies from the series of isolated short papers in the C.R. There does seem every warrant to support your hypothesis that the colicinogenic factor is extranuclear in its transmission.

1 May I ask you the favor of sending me a reprint ot two of this paper (for teaching purposes) together with your papers since early 1954?

I am particularly interested in the analogy between colicinogeny and F, the parallel behavior of which agents suggesting that they are each extranuclear. Although Jacob believes that F is simply a terminal (proximal) marker on the chromosome, the nonlinkage of F to colicinogeny implies that at least one of these, and possibly both, is extrachromosomal. I have long felt that the very high efficiency of F contagion, and its ability to spread thrsough an F^- population, argued strongly for its plasmid nature. This is supported by some very recent experiments I have been doing on conjugation of single F^+/F^- pairs. Unlike every other marker, ~~xxxxxxx~~ which shows several generations of segregation in the ♀ exconjugant clone, the converted F^+ clones are immediately pure for this trait.

It would be advantageous to conduct similar experiments in which a colicinogenic factor was also being trahsmitted concordantly. I am on the point of developing some strains suitable for such experiments, but with your assistance I might be able to save some time. Judging from your account, I could best introduce these factors into my various stocks if I had a K-12 auxotroph, F^+, and carrying the factor in question. Could I impose upon you for such stocks? Might I also ask for
2 the most suitable indicator, conveniently carrying the S^r mutation?

Another question of some interest I already raised at London: the possible ~~xxxxx~~ reciprocal transfer of colicinogeny: one wonders if there might ~~b~~ not be some conditions where it was possible. Are you
3 studying this further? Can you~~b~~ tell me the types of experiments that have been tried? E.G. Hfr x F^- K , or Hfr x F^+ K

Already in writing this letter, I have sensed the need for an explicit terminology for colicinogenic factors. The analogy between these and the kappa-paramecin story in Paramecium seems so precise that one would be justified in ~~xxxxxx~~ adopting a Greek-letter symbol, as is customary genetic convention for plasmids, for the colicinogenic factor. I would leave it to your judgment whether to go so far as to use the same letter K with appropriate subscripts, e.g. K_A, K_B, etc. or whether it would be more cautious to use another. It would simplify
4 discussions to have such symbols; you are clearly the person to introduce them. (In retrospect, it appears that λ was a mistake, since, mirabile dictu, this proves to be chromosomally inherited!) I am pondering whether we should also do this with F, in order to mitigate the confusion from F^+ as a denotation of mating type with F^+ as a symbol

for the carriage of the contagious factor. However, the relationships between the Hfr and F elements need further clarification. An attractive hypothesis, for which there is some support, is that Hfr represents the fixation of the F plasmid to a chromosomal site -- we have some fragments of new data since our original account of mating types when this was forwarded -- perhaps in analogy to the wanderings of McClintock's 'dissociator' factor in maize. Have you had any indication of such a phenomenon with the "kappas"? It might be manifest as a transformed cell (strictly speaking, a cell cannot be transduced, it is the genetic factor which is transduced, my own grammatical errors on this point notwithstanding) which is not colicinogenic, or which is not an infective source of kappa, but which is immune to the colicin.

This letter is full of questions, n'est-ce pas? To speed your answering them, I will have numbered them. But I have one more. It has, I believe, been some time since you last visited the United States. Have you given any thought to the possibility of coming again for six months or a year ? If this does become a possibility for you, and if it would appeal to you, perhaps we might begin a discussion of your visiting our laboratory as an honored guest. I am not proposing this for the immediate future, but perhaps for some time, say, in 1959. Meanwhile, with all best wishes for a happy Christmas and a fruitful New Year,

Sincerely,